

Gonadotropic Hormones

LH & FSH

Dept. of Pharmacology, GMC
Amritsar

1

Hypothalamus

GnRH

Ant. Pituitary

⊕ ↓ *-ve*
LH]
FSH] ⊕, *-ve*

Target tissue

⊕ ↓ *-ve*
Gonads

Target tissue Product

⊕ Sex steroids Inhibin

Secondary Target tissue

Accessory sex organs Other tissues

Hypothalamic-pituitary-gonadal axis.

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2

Molecular & Cellular Basis Of Gonadotropin Action

- LH & FSH named due to their actions on ovary.
- Actions of LH mediated by LH receptors (gene on chromosome 2p21)
- FSH by FSH receptor (gene on Chr. 2q)
- LH-FSH, GPCR, Large extracellular domain have high affinity & specificity.
- FSH & LH receptors couple with $GS\alpha$, \uparrow adenylyl cyclase, \uparrow cAMP.
- At high conc., agonist-occupied gonadotropin receptors \uparrow PKC & \uparrow Ca signaling pathways.

Physiological Effects Of Gonadotropins

- In Men, LH acts on Leydig cells to \uparrow de novo synthesis of androgens, the testosterone.
- Testosterone – Spermatogenesis within seminiferous tubules, maintenance of libido & secondary sexual characteristics.
- FSH acts on sertoli cells to \uparrow production of proteins & nutrients required for sperm maturation.

.....Physiological Effects

- Women, FSH \uparrow growth of developing ovarian follicles & induces expression of LH receptors on theca & granulosa cells.
- FSH regulates aromatase in granulosa cells, \uparrow 17 β -estradiol.
- LH – theca cells \uparrow Androstenedione – precursor of 17 β -estradiol.
- LH – rupture of dominant follicle during ovulation & progesterone synthesis by corpus luteum.

Diagnostic Uses Of Gonadotropins

- **Pregnancy diagnosis.**
- **Prediction of ovulation** – Ovulation occurs 36 hrs after onset of LH surge (10-12 hrs after peak of LH), urinary conc. can be used to predict ovulation, urine LH levels, 12-24 hrs, begin on day 11 of the cycle (assuming 28 day cycle). Such estimates facilitate timing of sexual intercourse to achieve pregnancy.

.....Diagnostic Uses

- Diagnosis of diseases of male & female reproductive system.
 - Hypogonadotropic hypogonadism - low levels of LH & FSH
 - High levels – primary gonadal disease.
 - Amenorrhoea in women or delayed puberty in men & women.
- Plasma LH-FSH levels.
- FSH \geq 15 IU/ml – reduced fertility, ↓ success in IVF.

Gonadotropins Preparations

- CG mimics LH – urine of pregnant female.
- Menotropins – urine of PM women equal amounts of LH & FSH.
- Urofollitropin (UFSH) – purified FSH.
- Highly purified FSH – immunoconcentration with monoclonal antibodies.
- rFSH – Follitropin α & Follitropin β , efficacious, lower frequency of ovarian hyperstimulation.

Therapeutic Uses

- Female Infertility – Gonadotropins in ART.
- Anovulating women with Hypogonadotropic hypogonadism secondary to hypothalamic or pituitary disease – class I anovulation.
- Polycystic ovarian disease not responding to clomiphene (Class II)
- Infertile women despite normal ovulation.

.....Therapeutic Uses

- FSH 75 IU daily until cycle day 6 or 7, assess ovarian response by transvaginal U/S – No. & size of developing follicles, every 2-3 days, >18mm follicle diameter. If >16mm (3 or 4), contraception to prevent multiple pregnancies & OHSS.
- s/estradiol level measurement. Target range 500-1500 pg/ml. If ovarian response imparted, ↑ dose FSH 150 IU daily.
- Inj. CG (5000-10000 IU) one day after last dose of gonadotropin for completing follicular maturation & ovulation.

.....Therapeutic Uses

- 10-20 % cases, multiple births due to release of more than one ovum.
- ART (IVF) & intra cytoplasmic sperm injection (ICSI) – FSH - for follicular maturation.
 - mature eggs surgically retrieved from preovulatory follicles.
 - Retrieved ova are fertilized in vitro with sperm or by sperm injection & transferred to uterus or fallopian tubes.

Side Effects

- Multiple births.
- **Ovarian Hyperstimulation Syndrome** – Rapid accumulation of fluid in peritoneal cavity, thorax, pericardium.
- Signs & symptoms:
 - Abdominal pain &/or distension.
 - N,V,D.
 - Marked ovarian enlargement.
 - Dyspnoea.
 - Oliguria, Hypovolemia
 - Electrolyte abnormalities
 - Ascites
 - Pleural effusion
 - Thromboembolism.

Clinical Uses

- **Male Infertility**

- CG (1000-5000 IU) i.m. thrice weekly till plasma conc. of testosterone establishes full steroidogenesis.
- CG dose 2000 IU twice weekly.
- Inj Menotropin (LH-FSH) 75 IU – 150 IU to induce spermatogenesis.

Side effect - Gynaecomastia

- **Cryptorchidism not secondary to anatomical blockage**- Inj CG 3000 U/m of body surface area IM every other day X 6 doses / Orchiopexy.

Thank You